MEDICAL MUTUAL®

Drug Policy

Policy:	Kalydeco (ivacaftor)	Annual Review Date: 06/20/2024 Last Revised Date: 06/20/2024

OVERVIEW

Kalydeco, a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator, is indicated for the treatment of cystic fibrosis (CF) in patients ≥ 1 month of age who have who have one mutation in the CFTR gene that is responsive to Kalydeco potentiation based on clinical and/or *in vitro* assay data. Mutations with an increase in chloride transport of 10% or greater are considered responsive.[1] In patients with unknown genotype, a FDA-cleared CF mutation test should be used to detect the presence of the CFTR mutation followed by verification with bidirectional sequencing when recommended by the mutation test instructions for use. Kalydeco is not effective in patients with CF who are homozygous for the F508del mutation in the CFTR.[1] A patient must have at least one CFTR mutation responsive to ivacaftor to be indicated. Table 1 lists mutations that are responsive to Kalydeco.

Table 1. List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Kalydeco.[1]

2789+5G—>A	*F311del*	*I148T*	*R75Q*	*S549N*
3272-26A—>G	*F311L*	*I175V*	*R1070Q*	*S549R*
3849+10kbC—>T	*F508C*	*I807M*	*R1070W*	*S945L*
711+3A—>G	*F508C;S1251N*	*I1027T*	*R117C*	*S977F*
A120T	*F1052V*	*I1139V*	*R117H*	*S589N*
A234D	*F1074L*	*K1060T*	*R347H*	*S737F*
A349V	*G1069R*	*L206W*	*R352Q*	*S1159F*
A1067T	*G1244E*	*L320V*	*R117G*	*S1159P*
A455E	*G1349D*	*L967S*	*R117L*	*T338I*
D110E	*G178R*	*L997F*	*R117P*	*T1053I*
D1152H	*G551D*	*L1480P*	*R170H*	*V232D*
D11OH	*G551S*	*M152V*	*R347L*	*V562I*
D192G	*G194R*	*M9521*	*R553Q*	*V754M*
D1270N	*G314E*	*M952T*	*R668C*	*V1293G*
D924N	*G576A*	*P67L*	*R792G*	*W1282R*
D579G	*G970D*	*Q237E*	*R933G*	*Y1014C*
E193K	*Y1032C*	*Q237H*	*R1162L*	*G178E*
E882K	*G1249R*	*Q359R*	*R1283M*	
E56K	*H939R*	*Q1291R*	*S1251N*	
E831X	*H1375P*	*R74W*	*S1255P*	

CFTR – Cystic fibrosis transmembrane regulator.

POLICY STATEMENT

This policy involves the use of Kalydeco. Prior authorization is recommended for pharmacy benefit coverage of Kalydeco. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval**

for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Kalydeco as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Kalydeco be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Kalydeco is recommended in those who meet the following criteria:

1. **Cystic Fibrosis (CF); Initial Therapy**
   Criteria. *Patient must meet the following criteria (A, B, and C):*
   - **A)** The patient has at least one mutation of the cystic fibrosis transmembrane conductance regulator (CFTR) gene that laboratory testing shows is susceptible to treatment with Kalydeco (Note: See Table 1 above for list of mutations); AND
   - **B)** The patient is ≥ 1 month old; AND
   - **C)** Kalydeco is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of CF.

2. **Cystic Fibrosis; Continuation of Therapy**
   Criteria. *Patient must meet the following criteria (A and B):*
   - **A)** Kalydeco is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of CF; AND
   - **B)** The patient has experienced a beneficial response to therapy such as increase in weight; improvement in sweat chloride; improvement in predicted FEV1 or other lung function tests; decrease in amount/frequency of pulmonary exacerbations; decrease in amount/frequency of pulmonary infections; decrease in hospitalizations.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Kalydeco has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

MEDICAL MUTUAL®

Drug Policy

1. **Cystic Fibrosis (CF), Patients who are Homozygous for the phe508del (F508del) Mutation in the Cystic Fibrosis Transmembrane Regulator (CFTR) Gene.** Efficacy results from a double-blind, placebo controlled trial in patients with CF who were homozygous for the phe508del mutation in the CFTR gene showed no statistically significant difference in FEV_1 over 16 weeks of Kalydeco treatment compared with placebo. In a Phase II trial in patients homozygous for the F508del (n = 112) Kalydeco did not result in an improvement in FEV_1 relative to placebo.

2. **Cystic Fibrosis (CF), Patients with Unknown Cystic Fibrosis Transmembrane Regulator (CFTR) Gene Mutation.** A Food and Drug Administration (FDA)-cleared CF mutation test should be used to detect the presence of the CFTR mutation prior to use of Kalydeco.

3. **Combination Therapy with Orkambi, Symdeko, or Trikafta.** Orkambi, Symdeko, and Trikafta contain ivacaftor, the active agent in Kalydeco and therefore are not indicated in combination with Kalydeco.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Kalydeco® tablets and oral granules [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals, Inc; August 2018.
2. Farrell PM, Rosenstein BJ, White TB, et al. Guidelines for diagnosis of cystic fibrosis in newborns through older adults: Cystic Fibrosis Foundation consensus report. *J Pediatr*. 2008;153:S4-S14.
3. De Bock K, Munck A, Walker S, et al. Efficacy and safety of ivacaftor in patients with cystic fibrosis and a non-*G551D* gating mutation. *J Cyst Fibros*. 2014;13:674-680
4. Cystic Fibrosis Foundation Annual Report. Available at: http://www.cff.org/UploadedFiles/aboutCFFoundation/AnnualReport/2013-Annual-Report.pdf. Accessed on: August 7, 2017.
5. Ivacaftor. In: DRUGDEX [online database]. Truvem Health Analystics; Greenwood Village, CO. Last updated 28 September 2020. Accessed on 7 October 2020.
6. Institute for Clinical and Economic Review (ICER). Modulator Treatments for Cystic Fibrosis: Effectiveness and Value. May 3, 2018.